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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
COTTON, ABIGAIL MANDA	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 10/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/509,839	FUKUNAGA ET AL.	
	Examiner	Art Unit	
	Abigail M. Cotton	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/30/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-17 are pending in the application as of the preliminary amendment filed on September 30, 2004.

Priority

Applicant's claim of foreign priority to JAPAN 2002-98977 04/01/2002 is acknowledged.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating periodontal disease, does not reasonably provide enablement for preventing periodontal disease, as recited in claim 9. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without ***undue experimentation***. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Foreman*, 230 USPQ 546 (Board of Appeals 1986) at 547, the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art: (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation that is necessary.

(1) *The Nature of the Invention:*

The invention is drawn to a method of treating or preventing periodontal disease by administering a viscous preparation comprising basic fibroblast growth factor and a thickener.

(2) *Breadth of the Claims:*

The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims. The claimed invention includes the treatment and

prevention of all periodontal disease. The term "prevention" indicates a claim whereby those normally not at risk for developing such a condition would be prevented from ever developing the condition with the composition being claimed.

(3) ***Guidance of the Specification:***

The guidance of the specification as to "preventing" periodontal disease is completely lacking. Note for example in Test Example 4 of the Specification, the viscous preparation is administered to a defect portion at the right side mandibula of a rabbit. The amount of bFGF present 6 hours of administration was then measured, and it was demonstrated that the viscous composition remains at the administered area for a long period of time. In Test Example 3 of the Specification, the viscous composition administered to the left hind leg of rats was also shown to remain at higher amounts in the administered portion after 6 hours, as compared to that of a standard aqueous solution of bFGF. Accordingly, the specification shows that the viscous composition is capable of being retained in an administered area for a long period of time, such as 6 hours. The specification also teaches that longer local retention at an administered area provides better treatment (see page 4, second full paragraph, in particular.) However, the specification does not provide any guidance as to whether the viscous composition *prevents* all types periodontal disease. The specification also does not provide any alternative models by which the prevention of periodontal disease could be assessed.

(4) ***Working Examples:***

As discussed in the Guidance of the Specification section above, Applicant has only shown examples for the increased stay of the viscous preparation at an administration site for treatment. Applicant has not shown examples for the complete *prevention* of all periodontal diseases.

(5) ***State of the Art:***

The state of the art regarding *treating* of periodontal disease is well developed. However, the state of the art regarding *preventing* of periodontal disease is underdeveloped (see for example U.S. Patent Application Publication No. 2003/0035779 to Brown et al.) Brown et al. describes how periodontal disease is caused at least in part by biofilms (aged plaque), which are notoriously difficult to remove (see paragraph 0003, in particular.) Brown et al. describes that the current oral hygiene response is ineffective, as is demonstrated by the size of the U.S. periodontal market (see paragraph 0004, in particular.) Thus, Brown et al. shows that it is known to treat periodontal disease, for example by removing biofilms, but the compete prevention of periodontal disease is not known.

Reasonable guidance with respect to *preventing* periodontal disease relies on quantitative analysis from defined populations that have been successfully pre-screened and are predisposed to such conditions. This type of data might be derived from widespread genetic analysis, family histories, correlation of genetic and environmental factors, etc. The essential element towards the validation of a preventive therapeutic is the ability to test the therapeutic on subjects monitored in advance of the onset of periodontal disease, and *link* those results with subsequent histological confirmation of the presence or absence of periodontal disease. This irrefutable link between antecedent drug and subsequent knowledge of the prevention of the condition is the essence of a valid preventive agent. As the correlation among factors contributing to the rise of biofilms and/or periodontal disease are not known, the state of the art does not provide a reasonable method of making such a predictive analysis. Further, a preventive administration also must assume that the therapeutic will be safe and tolerable for anyone susceptible to the condition or disease.

(6) *Predictability of the Art*

The invention is directed to treating or *preventing* periodontal disease in *general* with a composition having bFGF and a thickener. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *in re Fisher*, 427 F.2d 833, 839 (1970.)

It should also be noted that one of ordinary skill in the art would recognize that it is highly unpredictable in regard to what population will experience periodontal disease, as discussed in (5) above. In order to administer the agent to the population at large, one would need to consider the therapeutic effects, side effects and especially potential serious toxicity that may be generated by drug-drug interactions as a result of administration of the claimed compounds to a living organism (e.g., an animal.)

(7) ***The Quantity of Experimentation Necessary:***

In order to practice the disclosed invention, one would need to undergo experimentation to test compositions with bFGF and a thickener such as those claimed to determine whether or not any of them are actually capable of completely preventing periodontal disease, as the instant specification does not show the complete prevention thereof.

As discussed above, the specification fails to provide sufficient support for determining all individuals susceptible to periodontal disease to allow one or ordinary skill in the art to administer to a population the bFGF composition of the instant invention for the *prevention* of periodontal disease in general. As a result, one of ordinary skill in the art would be forced to perform an exhaustive search for the population that is susceptible to periodontal disease to use the instant invention.

Genentech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

The Examiner suggests deleting the reference to "preventing" in claim 9. For examination purposes, the Examiner is interpreting the claims as drawn to a method of treating periodontal disease.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by EP 0 267 015 to Amy L. Finkenaur, published May 11, 1988.

Finkenaur teaches that medicinal compositions containing a polypeptide growth factor having mitogenic activity are stabilized against loss of biological activity in the

presence of moisture by including a stabilizing amount of a water-soluble polysaccharide in the composition (see abstract, in particular.) Finkenaur teaches that basic fibroblast growth factor an example of such as polypeptide growth factor that can be stabilized with the polysaccharide (see page 3, lines 25-30, in particular.) Finkenaur further teaches that the polysaccharides act to increase the viscosity of the composition (see page 4, lines 55-65, in particular), and thus are thickeners. Accordingly, Finkenaur teaches a composition comprising a basic fibroblast growth factor and a thickener, as recited in claim 1.

It is respectfully pointed out that the recitation "for dental use" in claim 1 has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *in re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and Kropa v. Robie, 187 F.2d 150, 152 88 USPQ 478, 481 (CCPA 1951.)

Furthermore, regarding claim 4, it is respectfully pointed out that a recitation of an intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the

intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963.) Thus the intended use recited in claim 4, namely that the viscous preparation is "for treatment of periodontosis" is not afforded patentable weight.

Accordingly, the teachings of Finkenaur anticipate the compositions of claims 1 and 4.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2-3 and 5-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0 267 015 to Amy L. Finkenaur, published May 11, 1988.

Finkenaur is applied as discussed for claim 1 and 4 above and teaches a composition comprising a polypeptide growth factor, such as basic fibroblast growth

factor, with a polysaccharide thickener that acts to stabilize the growth factor in the presence of moisture.

Finkenaur does not provide a specific example of a composition having basic fibroblast growth factor and one of the thickeners claimed in claims 2-3. Finkenaur also does not teach a specific example of a composition having basic fibroblast growth factor in the percent by weight as recited in claim 5. Finkenaur et al. also does not provide a specific example of a kit as in claim 6, and does not teach a specific example of dissolving bFGF and a thickener to form the claimed composition, as recited in claims 7-8.

Regarding claims 2-3, Finkenaur teaches that the stabilizing polysaccharide for stabilizing the polypeptide growth factor can be selected from among polysaccharides including methyl cellulose, hydroxyethylcellulose and hydroxypropyl methylcellulose, as in claim 2, and hydroxypropyl cellulose, as in claim 3 (see page 3, lines 35-50, in particular.) Accordingly, one of ordinary skill in the art at the time the invention was made would have found it obvious to provide one of the polysaccharides taught by Finkenaur with bFGF to form the composition of claim 2 or 3, with the expectation of providing a polysaccharide-stabilized composition of bFGF.

Regarding claim 5, Finkenaur teaches that the composition can comprise growth factor in an amount of from about 0.01 to about 1000 micrograms per milliliter of

aqueous formulation (see page 4, lines 15-20, in particular), and teaches other formulations such as dietary supplements and opthalmic formulations having other suitable contents of the growth factor (see page 4, lines 30-65, in particular.) Accordingly, it is considered that one of ordinary skill in the art at the time the invention was made would have found it obvious to vary and/or optimize the amount of bFGF in the formulation to provide a desired stabilized composition having mitogenic activity. It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955.)

Regarding claim 6, Finkenaur provides examples of formulations formed by combining a growth factor and polysaccharides (thickeners) in a water-containing solution (see Examples 1-3, in particular.) Finkenaur also teaches that bFGF is a suitable growth factor, as discussed above. Accordingly, one of ordinary skill in the art at the time the invention as made would have found it obvious to provide the bFGF, polysaccharide and a solution for dissolution together, for example as a kit, with the expectation of providing components suitable for forming a stabilized growth factor composition with mitogenic activity.

Regarding claims 7-8, Finkenaur teaches that the composition can be prepared by providing a polypeptide growth factor such as bFGF, in an aqueous medicinal composition such as a gel, solution, suspension or dispersion, in which is dissolved an effective amount of the water soluble polysaccharide (see column 3, lines 55-60, in

particular.) Accordingly, one of ordinary skill in the art at the time the invention was made would have found to obvious to prepare the composition by dissolving the bFGF and thickener in a solution (such as water), because Finkenaur teaches that a suitable method of forming the composition comprising providing an aqueous solution of the bFGF, in which the thickener (polysaccharide) can be dissolved.

It is respectfully pointed out that the recitation "for dental use" in claims 2-3 and 5-8 has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *in re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and Kropa v. Robie, 187 F.2d 150, 152 88 USPQ 478, 481 (CCPA 1951.)

Claims 9-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,046,164 to Asano et al, issued April 4, 2000, in view of EP 0 267 015 to Amy L. Finkenaur, published May 11, 1988.

Asano et al. teaches a method for treating diseases of periodontal tissue by administering a basic fibroblast growth factor (see abstract, in particular.) Asano et al. teaches that the bFGF can be prepared in various formulations, including liquids by

combining bFGF with a pharmacologically acceptable additive, such as a solvent, stabilizer, etc. (see column 4, lines 4-15, in particular.)

Asano et al. does not specifically teach providing a thickener in the bFGF composition.

Finkenaur teaches that a stabilizing effective amount of a water-soluble polysaccharide can be provided in medicinal compositions containing a polypeptide growth factor with mitogenic activity to stabilize the polypeptide growth factor against loss of biological activity in the presence of moisture (see abstract, in particular.) Finkenaur teaches that basic fibroblast growth factor is an example of such as polypeptide growth factor that can be stabilized with the polysaccharide (see page 3, lines 25-30, in particular.) Finkenaur further teaches that the polysaccharides act to increase the viscosity of the composition (see page 4, lines 55-65, in particular), and thus are thickeners.

Accordingly, one of ordinary skill in the art at the time the invention was made would have found it obvious to incorporate the stabilizer/thickener of Finkenaur into the bFGF composition taught by Asano et al. and administer for the treatment of periodontal disease, because Asano et al. teaches that a composition comprising bFGF and a stabilizer can be administered for the treatment of periodontal disease, and Finkenaur teaches that polysaccharides (that are also thickeners) act to stabilize bFGF. Thus, one

of ordinary skill in the art would have been motivated to provide the polysaccharide of Asano et al. in the bFGF composition of Asano et al. for administration with the expectation of administering a stabilized formulation capable of treating periodontal disease. Therefore, the method of claim 9 is obvious over the teachings of Finkenaur and Asano et al.

Regarding claims 10-11, Finkenaur teaches that the stabilizing polysaccharide for stabilizing the polypeptide growth factor can be selected from among polysaccharides including methyl cellulose, hydroxyethylcellulose and hydroxypropyl methylcellulose, as in claim 10, and hydroxypropyl cellulose, as in claim 11 (see page 3, lines 35-50, in particular.) Accordingly, one of ordinary skill in the art at the time the invention was made would have found it obvious to provide one of the polysaccharides taught by Finkenaur in the bFGF composition of Asano et al. to form and administer the composition of claim 10 or 11, with the expectation of providing a polysaccharide-stabilized composition of bFGF capable of treating periodontal disease.

Regarding claims 12 and 15, Asano et al. teaches that the bFGF composition can treat periodontitis (periodontosis.) Regarding claims 13-14 and 16, Asano et al. teaches that a suitable content of bFGF in the composition can be from 0.001 to 20%, which is the same as the ranges being claimed. Regarding claim 17, Asano et al. teaches that the composition can be administered for repair of periodontal tissue after

tooth extraction, and for regeneration of dentin defected by dental caries, as recited in the claim.

Accordingly, the invention as recited in claims 9-17 is obvious over the teachings of Asano et al. and Finkenaur.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abigail M. Cotton whose telephone number is (571) 272-8779. The examiner can normally be reached on 8:30-5:00, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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AMC

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